

16955DIVCONCIP(AP)PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:
Woodward et al

Serial No: 08/605,567

Filed: February 22, 1996

For: CYCLOPENTANE HEPTANOIC
ACID, 2-CYCLOALKYL OR
ARYLALKYL DERIVATIVES AS
THERAPEUTIC AGENTS

Group No. : 1209

Examiner: M. Cebulak

APPROVED

RECEIVED
9/10/98DECLARATION UNDER 37 CFR 1.131

Honorable Commissioner of Patents
and Trademarks
Washington, D.C. 20231

Dear Sir:

The Declarant hereby declares as follows:

THAT, he is currently employed by Allergan, Inc. in the
Department of Biological Sciences, Pharmaceutical Research &
Development;

THAT, he has been employed at Allergan since 1982;

THAT, his research is in the field of glaucoma, in
particular the effect of prostaglandin derivatives on
lowering intraocular pressure, among other fields;

THAT, he obtained a Ph.D. degree (Pharmacology) from
CNAAL, Leicester School of Pharmacy 1980;

THAT, he obtained a B.S. (Pharmacology) in 1975;

16955DIVCONCIP(A)
Serial No. 08/605,567

2

THAT, he is named as an inventor in the above-identified patent application;

THAT, he directed and supervised the following experiments, in the United States of America, prior to August 3, 1993, the filing date of U.S. Patent Number 5,510,383 to Bishop;

THAT, as described in Example 6, of U.S. Patent Number 5,352,708, i.e. the parent application of the present application, the effectiveness of AGN 192185 in lowering intraocular pressure (IOP) in dogs was measured;

THAT, AGN 192185 is the 1-CONH₂ derivative of fluprostenol;

THAT, as shown in Exhibit A, which is a true copy of page 85 of his Notebook (with only the dates blocked out) and is attached hereto and made a part hereof, a 0.1% solution of AGN 192185 in a vehicle was prepared and designated as 185B;

THAT, as shown in Exhibit B, which is a true copy of page 86 of his Notebook (with only the dates blocked out) and is attached hereto and made a part hereof, 185B was topically applied to one eye of eight dogs and the lowering of IOP in that eye over 24 hours was measured;

THAT, in Dog Numbers KHD2, KID2, AC2 and KLC2 the IOP in the eye that received 185B was lowered;

THAT, as shown in a graph format in Exhibit C, which is a true copy of page 20 of his Notebook (with only the dates blocked out) and is attached hereto and made a part thereof, 0.01% fluprostenol when tested as described in Example 6 of U.S. Patent Number 5,352,708 also shows a lowering of the IOP in dogs;

16955DIVCONCIP (AP)
Serial No. 08/605,567

3

THAT, as shown in a graph format in Exhibit D, which is a true copy of page 15 of his Notebook (with only the dates blocked out) and is attached hereto and made a part thereof, 0.1% fluprostenol when tested as described in Example 6 of U.S. Patent Number 5,352,708 also shows a lowering of IOP in dogs;

THAT, the results reported in Exhibits A through D clearly demonstrate that topical administration of fluprostenol and derivatives thereof lower IOP;

The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully,

4.23.97

Date


David F. Woodward

85

EXHIBIT A

Title ICP- DOGS

Project Name _____

Project No. _____

Enter Purpose, Method, Results and
Conclusions for each Study.

Date _____

Sample I.D. No. _____

Book No. _____

Continued from _____

Purpose: see page 9.Method: see pages 1-9.Drug Preparation: see page 9.Drug Code:

C. 17 AGN 192185

185A = vehicle

185B = drug

Rabbit Test:

rabbit # 27 (R) eye

2 = 30 min. eye clear + rabbit in good health

Notes:

OSH

Study done on 11/2/92

DOG KID₂

was + 2.5 - had swelling

-75

DOG AC₂

had severe ptosis

1.0

1.25

.50

1.0

.50

.75

.75

6.5/8 = 81

Continued on 86

Signature Linda Williams

Date _____

Read & Understood by Jan Beltranda

Date _____

BEST AVAILABLE COPY

Title _____
Project Name Vanu 0485
Project No. _____
Enter Purpose, Method, Results and
Conclusions for each Study.

Date _____
Sample I.D. No. _____
Book No. _____
Continued from _____

Drug Number	Eye	T=0 IOP \pm SD	T=2 IOP \pm SD	T=4 IOP \pm SD	T=6 IOP \pm SD	T=24 IOP \pm SD
(A)	L	12.0 \pm .3	15.6 \pm .6	13.4 \pm .5	11.4 \pm .4	14.2 \pm .7
2002 (B)	R	13.1 \pm .2	13.4 \pm .6	14.3 \pm .6	10.1 \pm 1.0	14.6 \pm .6
KHD2	L	12.7 \pm .4	12.0 \pm .4	15.1 \pm .8	14.2 \pm .1	14.7 \pm .7
	R	12.5 \pm .1	2.2 \pm .7	8.8 \pm .5	0.7 \pm .7	10.9 \pm .1
KID2	L	13.5 \pm .1	12.8 \pm .5	13.3 \pm .9	14.0 \pm .2	10.1 \pm .3
	R	13.4 \pm .1	7.3 \pm .1	7.1 \pm .6	11.2 \pm .1	2.8 \pm .5
KUD2	L	13.7 \pm .3	14.9 \pm .6	12.0 \pm .3	12.9 \pm .2	13.3 \pm .9
	R	16.2 \pm .4	14.3 \pm .1	12.8 \pm .3	13.9 \pm .3	16.1 \pm .7
KPD2	L	15.3 \pm .7	10.3 \pm .3	10.6 \pm .2	12.6 \pm .2	12.4 \pm .5
	R	18.5 \pm .6	15.1 \pm .8	14.0 \pm .7	16.8 \pm .6	13.1 \pm .2
ACL2	L	17.5 \pm .7	13.5 \pm .5	16.8 \pm .5	20.1 \pm .8	12.1 \pm .6
	R	18.4 \pm .7	15.7 \pm .1	13.4 \pm .6	13.4 \pm .7	15.5 \pm .1
KL02	L	15.5 \pm .7	12.4 \pm .1	18.7 \pm .4	17.7 \pm .6	15.5 \pm .3
	R	15.9 \pm .6	14.4 \pm .7	15.2 \pm .3	13.2 \pm .3	12.8 \pm .2
IP02	L	16.6 \pm .6	15.9 \pm .3	14.2 \pm .3	12.7 \pm .9	12.0 \pm .7
	R	14.6 \pm .9	15.5 \pm .7	16.3 \pm .8	13.7 \pm .5	13.2 \pm .3

Behrend account ^{copy} general VAX
8/10

0000000000 000 x 00

0.24 00000000

0 1 0.00 2 2.00 3 4.00 4 6.00 5 24.00

1	10.00	10.00	10.00	10.00	10.00
2	2.00	2.00	2.00	2.00	2.00
3	0.00	0.00	0.00	0.00	0.00
4	14.00	14.00	14.00	14.00	14.00
5	2.00	2.00	2.00	2.00	2.00
6	0.00	0.00	0.00	0.00	0.00
7	0.00	0.00	0.00	0.00	0.00
8	0.00	0.00	0.00	0.00	0.00
9	0.00	0.00	0.00	0.00	0.00
10	0.00	0.00	0.00	0.00	0.00
11	0.00	0.00	0.00	0.00	0.00
12	0.00	0.00	0.00	0.00	0.00
13	0.00	0.00	0.00	0.00	0.00
14	0.00	0.00	0.00	0.00	0.00
15	0.00	0.00	0.00	0.00	0.00
16	0.00	0.00	0.00	0.00	0.00
17	0.00	0.00	0.00	0.00	0.00
18	0.00	0.00	0.00	0.00	0.00
19	0.00	0.00	0.00	0.00	0.00
20	0.00	0.00	0.00	0.00	0.00
21	0.00	0.00	0.00	0.00	0.00
22	0.00	0.00	0.00	0.00	0.00
23	0.00	0.00	0.00	0.00	0.00
24	0.00	0.00	0.00	0.00	0.00
25	0.00	0.00	0.00	0.00	0.00
26	0.00	0.00	0.00	0.00	0.00
27	0.00	0.00	0.00	0.00	0.00
28	0.00	0.00	0.00	0.00	0.00
29	0.00	0.00	0.00	0.00	0.00
30	0.00	0.00	0.00	0.00	0.00

Continued on 87
Signature [Signature]

Read & Understood by [Signature]
Date _____

09/10/98 13:21

0714 0164249

AGN LEGAL DEPT

015/016

04/22/97 11:01

0714 015538

ALLERGAN

004

20

EXHIBIT C

Title

Project Name

Project No.

Enter Purpose, Method, Results and
Conclusions for each Study.

Date

Sample I.D. No.

Book No.

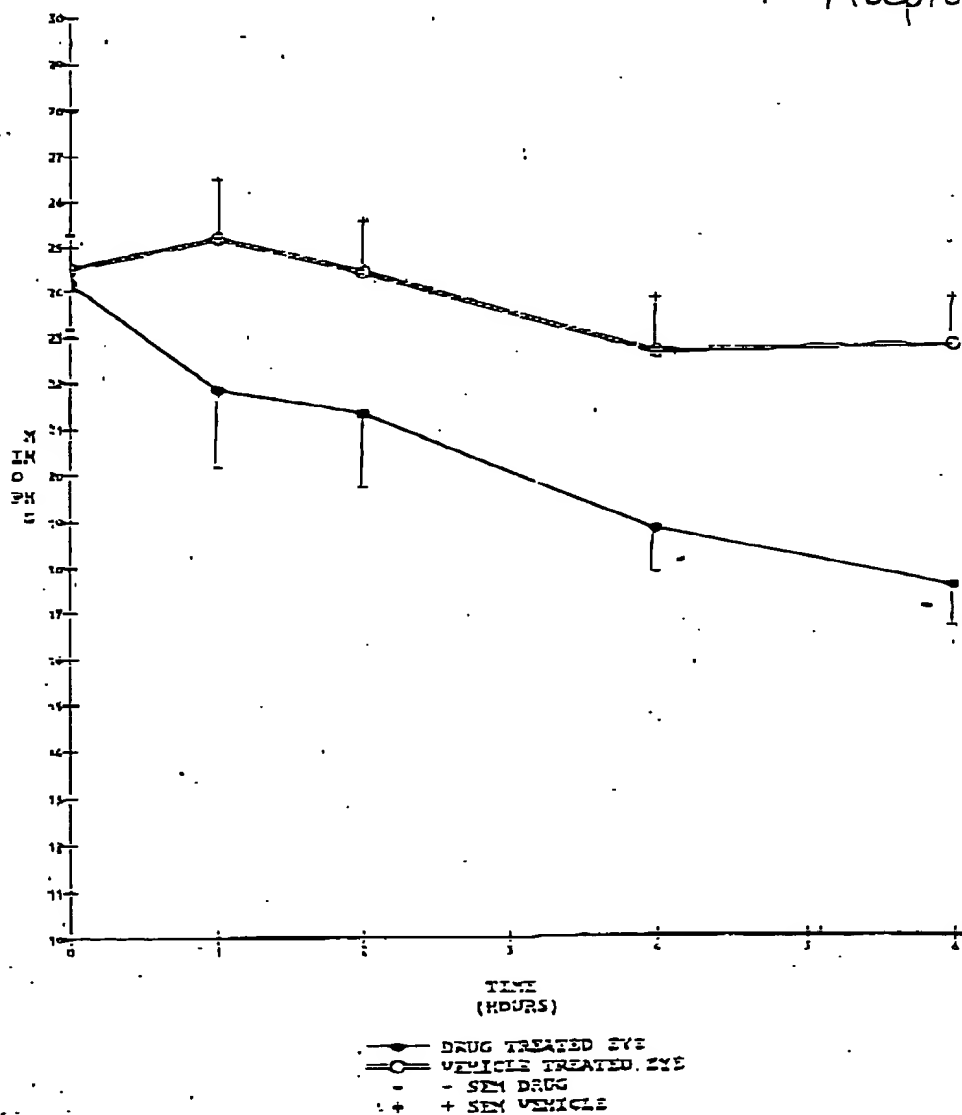
Continued from

AR925021001G

03-OCT-91 12:19 Page 1

935AB DOGS N=6

0.01% Fluorostanol



Continued on 21

Signature

Date

Read & Understood by Linda Williams

Date

09/10/98 13:22
04/22/97 11:01

8714 2464249
8714 16 5538

AGN LEGAL DEPT
ALLERGAN

016/016
005

15

EXHIBIT D

Title _____
Project Name Same as pg 13
Project No. _____
Enter Purpose, Method, Results and
Conclusions for each Study.

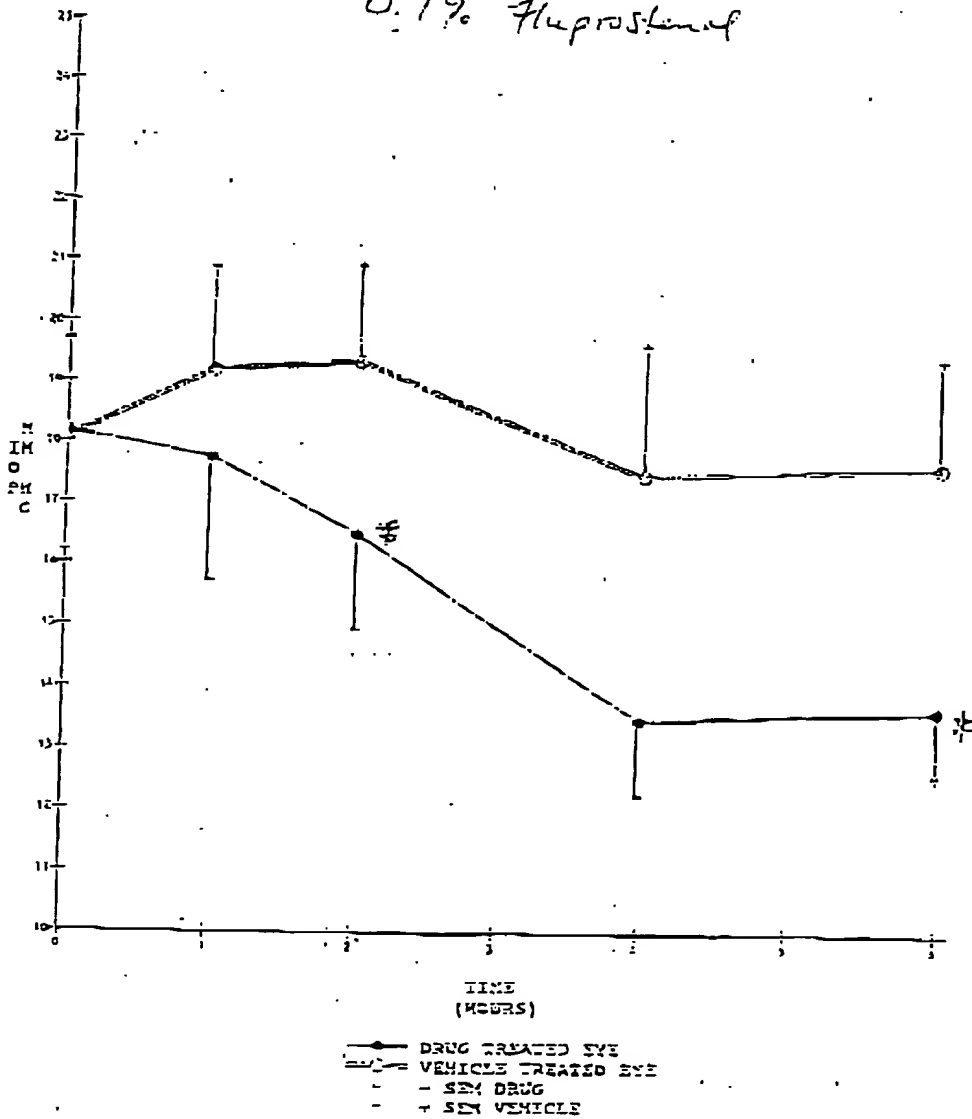
Date _____
Sample I.D. No. _____
Book No. _____
Continued from _____

1270210610

28-SEP-91 13:00 Page 1

DOG 107'924

0.1% Fluorometholone



Continued on pg 16
Signature [Signature]
Date 11

Read & Understood by [Signature]
Date _____